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10/036,828	12/21/2001	Tiecheng A. Qiao	82917WFN	4935

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,828	QIAO ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 27 October 2003 in which claims 1-2, 5, 7, 9, 21 and 23 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 25 July 2003 under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(e) and 35 U.S.C. 103(a) are maintained. New rejections, necessitated by the amendments are discussed below. All of the arguments have been thoroughly reviewed and are discussed below.

Claims 1-25 are under prosecution.

Specification

2. Applicant's amendment to the specification is acknowledged. However, the amendment deleting the paragraph beginning on page 17, line 6 does not place the specification in compliance with the Nucleic Acid Sequence rules. The paragraph beginning on page 17, line 6 includes lines 6-8. The deleted paragraph does not include Table 1 listing the nucleic acid sequences.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-18 and 21-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Walt et al (WO 00/16101, published 23 March 2000).

Regarding Claim 1, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at **random positions on the substrate** (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) wherein the microspheres are combined

randomly and in random distributions on the substrates (Abstract). Because the microspheres are randomly distributed, the substrate does not have preselected sites for association with the microspheres as newly claimed.

Regarding Claim 2, Walt et al disclose the method wherein each subpopulation has a unique optical signature (bar code) and a unique probe sequence (page 17, lines 15-19).

Regarding Claim 3, Walt et al disclose the method wherein the optical bar code is generated by two or more colorants i.e. each optical signature is comprises of a mixture of dyes (page 16, liens 25-28).

Regarding Claim 4, Walt et al disclose the method wherein the optical barcode is generated by a mixture of red, green and blue i.e. each optical signature is comprises of a mixture of dyes including red, green and blue dyes e.g. rhodamine, Malacite green, and Cascade Blue™ (page 16, line 25-page 17, line 2).

Regarding Claim 5, Walt et al disclose the method wherein at least one subpopulation has a luminescent property (i.e. fluorescence) and wherein detecting includes whole frame imaging capture of a resulting luminescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Regarding Claim 6, Walt et al disclose the method wherein said processing uses a pattern recognition algorithm to obtain the identification (page 32, line 5-page 35, line 12).

Regarding Claim 7, Walt et al disclose the method wherein at least one subpopulation has a fluorescent property and wherein detecting includes whole frame imaging capture of a resulting fluorescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Regarding Claim 8, Walt et al disclose the method wherein the substrate is characterized by an absence of specific sites capable of interaction physically or chemically with the microspheres i.e. a planar substrate or within a tube (page 7, liens 14-20).

Regarding Claim 9, Walt et al disclose the method wherein the microspheres bear surface active sites which contain the nucleic acid probe (page 14, lines 20-30).

Regarding Claim 10, Walt et al disclose the method wherein the microspheres have a mean diameter of between 1 and 50 microns (page 9, lines 21-23).

Regarding Claim 11, Walt et al disclose the method wherein the microspheres have a mean diameter of between 3 and 30 microns (page 9, lines 21-23).

Regarding Claim 12, Walt et al disclose the method wherein the microspheres have a mean diameter of between 5 and 20 microns (page 9, lines 21-23).

Regarding Claim 13, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 100 and 1 million microspheres per cm^2 (page 6, lines 21-24).

Regarding Claim 14, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 1,000 and 200,000 microspheres per cm^2 (page 6, lines 26-28).

Regarding Claim 15, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 10,000 and 100,00 microspheres per cm^2 (page 6, lines 21-28).

Regarding Claim 16, Walt et al disclose the method wherein the microspheres comprise a synthetic or natural polymeric material (page 9, lines 11-18).

Regarding Claim 17-18, Walt et al disclose the method wherein the microspheres comprise an amorphous polymer e.g. polystyrene (page 9, lines 11-18).

Regarding Claim 21, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a

population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) wherein at least one subpopulation has a luminescent property (i.e. fluorescence) and wherein detecting includes whole frame imaging capture of a resulting luminescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15) wherein the microspheres are combined randomly and in random distributions on the substrates (Abstract). Because the microspheres are randomly distributed, the substrate does not have preselected sites for association with the microspheres as newly claimed.

Regarding Claim 22, Walt et al disclose the method wherein said processing uses a pattern recognition algorithm to obtain the identification (page 32, line 5-page 35, line 12).

Regarding Claim 23, Walt et al disclose the method wherein each subpopulation has a unique optical signature (bar code) and a unique probe sequence (page 17, lines 15-19).

Regarding Claim 24, Walt et al disclose the method wherein the optical bar code is generated by two or more colorants i.e. each optical signature is comprises of a mixture of dyes (page 16, liens 25-28).

Regarding Claim 25, Walt et al disclose the method wherein the optical barcode is generated by a mixture of red, green and blue i.e. each optical signature is comprises of a mixture of dyes including red, green and blue dyes e.g. rhodamine, Malacite green, and Cascade Blue™ (page 16, line 25-page 17, line 2).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (a) (WO 00/16101, published 23 March 2000) in view of Walt et al (b) (U.S. Patent Application Publication No. 2002/0172716 A1, filed 25 October 2000).

Regarding Claim 19, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the

microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) but they do not teach the microsphere contains less than 30 percent crosslinking agent. However, Walt et al (b) teach microsphere composition whereby the amount of crosslinking agent determines microsphere pore size i.e. increasing amounts of crosslinking agents decreases pore size (¶ 7) and pores provide access to the hollow portion of the microsphere. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the microspheres for entrapping dye of Walt et al (a) with a percent crosslinking agent which provides appropriate access to the hollow portion of the microsphere for dye entrapment as suggested by Walt et al (b) for the obvious benefit of entrapping the optical signature-specific dyes.

7. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) in view of Chang et al (U.S. Patent No. 4,873,102, issued 10 October 1989).

Regarding Claim 20, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion,

polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) but they are silent regarding the polymerization method. However, emulsion polymerization preparation of microspheres was well known in the art at the time the claimed invention was made as taught by Change et al (Example 1, Column 6, lines 25-57) wherein the method provides microspheres of very narrow size range. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the emulsion polymerization of Change et al to the microspheres of Walt et al to thereby provide microspheres of a uniform size as taught by Chang et al (Column 6, lines 26-28) for the obvious benefits of providing consistent microsphere surface area for surface interaction and thereby controlling interaction uniformity.

Response to Arguments

8. Applicant argues that because Walt et al teach that the surface is modified to contain individual sites for attachment or association with the microspheres, they do not teach a substrate having no preselected sites for association with microspheres as newly claimed.

The argument has been considered but is not found persuasive because, as stated above, Walt et al specifically teach the microspheres are combined randomly and in random distributions on the substrates (Abstract). The fact that they teach an embodiment (cited by Applicant) wherein a site is preselected, does not alter the fact that they also teach no preselection.

Furthermore, the newly claimed no preselected sites is interpreted as requiring that no site (address) is selected for any specific microsphere prior to association of that microsphere with the site i.e. the association is random. Walt et al specifically teach the association is random (e.g. Abstract). Because the microspheres of Walt et al are randomly distributed, the substrate does not have preselected sites for association with the microspheres as newly claimed.

Applicant argues that the film forming polymers of Walt would not undergo sol-gel transition without solvent evaporation or chemical crosslinking as the instant invention. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., sol-gel transition without evaporation or crosslinking) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims are broadly drawn to a fluid containing a gelling agent or a precursor to a gelling agent. The claimed fluid encompasses a wide range of fluids including any agent which is a precursor to a gelling agent. Walt et al teaches the claimed fluid (page 22, lines 9-22).

NOTICE TO COMPLY WITH NUCLEIC ACID SEQUENCE RULES

9. This application ON PAGE 17 contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements

For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS GIVEN A PERIOD OF TIME CO-EXTENSIVE WITH THE PERIOD OF TIME TO REPLY WITH THE ABOVE OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. **Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g).** Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878 until 13 January 2004. Starting 14 January 2004, the examiner's phone number will be (517) 272-0741. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196. Starting 14 January 2003, the receptionist telephone number will be (517)-272-0507.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
December 29, 2003